II. REMARKS

Formal Matters

Claims 1-29 are pending after entry of the amendments set forth herein.

Claims 7-15 were examined and were rejected. Claims 1-6 and 16-22 were withdrawn from consideration.

Claims 23-29 are added. No new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Objection to the specification

The specification was objected to. The Office Action stated that the sequence identifiers need to be amended into the specification at page 36, lines 13 and 18, and at page 37, lines 1, 3, 28, and 30.

Applicants respectfully request entry of the above-noted amendments to the specification, which amendments adequately address the objection to the specification.

Rejection under 35 U.S.C. §112, first paragraph

Claims 7-15 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement.

The Office Action stated that the specification discloses that normal young (neonatal) healthy rat neurons from one ganglion of the peripheral nervous system, specifically neurons only from the superior cervical ganglion, can have their survival in tissue culture stimulated to only about 60% of what their survival would have been if nerve growth factor (NGF) had been used in the tissue culture. The Office Action stated that the method of the instant invention substitutes an agonist antibody for NGF *in vitro*, and the agonist antibody does not work as well as NGF. The Office Action asserted that there are no working examples of the instant method being used to treat any neurological disorder *in vivo*. Applicants respectfully traverse the rejection.

The instant specification provides ample guidance for use of a multivalent immunoglobulin (Ig) that binds a trk receptor on a cell, and activates the receptor. The instant specification provides ample guidance for use of such a multivalent Ig to promote an effector function of receptor activation, where effector functions include, e.g., promotion of neuronal survival, promotion of neuronal differentiation, and improved neuronal function. The fact that the specification provides ample support for use of a multivalent Ig to promote effector functions such as promotion of neuronal survival, promotion of neuronal differentiation, and improved neuronal function is shown by issuance of U.S. Patent No. 6,656,465, which claims a method for activating a trk receptor.

The Office Action noted that an agonist antibody that binds the NGF receptor trkA was less effective than NGF in promoting neuronal survival *in vitro*. However, such is not an indication of lack of enablement. The enablement requirement of 35 U.S.C. §112, first paragraph, does not require that a particular agent (in this case a multivalent Ig that binds and activates a trk receptor) work *better* than another agent, or even at least as well as another agent.

The Office Action stated that naturally occurring neurotrophins for the trk receptors have not been developed into any commercially available clinical therapies to treat any of the disorders recited in the instant claims. However, "development of commercially available clinical therapies" is not a requirement under 35 U.S.C. §112, first paragraph.

The Office Action stated that it is unpredictable how antibodies that are only 60% as effective as the naturally occurring neurotrophins are going to succeed in a predictable fashion when the neurotrophins themselves appear to be ineffective for treating any of the diseases recited in the instant claims.

The Office Action cited Olson et al. ((1993) *Exp. Neurol.* 124:5; "Olson"), and stated that Olson teaches that use of intraventricular NGF in one AD patient "did not results in any meaningful clinical treatment." Office Action, page 4. However, Olson actually states that several transient or more long-lasting improvements were noted in the pilot case, involving increases in blood flow, improvement of EEG, and improvement of certain psychological tests. Olson, Abstract; page 10, column 1, second and third full paragraphs; and page 10, bridging paragraph columns 1 and 2. Thus, Olson does not support a conclusion of lack of enablement. If anything, Olson tends to support the notion that trk agonists, such as NGF, would be efficacious in treating disorders such as AD.

Furthermore, Applicants note that the literature supports the notion that trk agonists, such as NGF, are useful for treating various disorders. Thus, those skilled in the art would find it reasonable to expect that other trk agonists, such as multivalent Ig that activate a trk receptor, would be efficacious in treating disorders.

For example, Tuszynski et al. ((2005) *Nat. Med.* 11:551; "Tuszynski") states that NGF "stimulates cholinergic function, improves memory and prevents cholinergic degeneration in animal models of injury, amyloid overexpression and aging." Tuszynski, Abstract. Tuszynski presents data from a phase 1 trial of *ex vivo* NGF gene delivery in eight individuals with mild AD, wherein autologous fibroblasts genetically modified to express human NGF into the forebrain were implanted into the individuals. Tuszynski states that the results suggested improvement in the rate of cognitive decline.

As another example, De Rosa et al. ((2005) *Proc. Natl. Acad. Sci. USA* 102:3811; "De Rosa") showed that intranasal administration of NGF rescued recognition memory deficits in a mouse model that exhibited certain features of AD.

Bowes et al. ((2000) *Brain Res.* 883:178) reported that intrathecal infusion of NGF reduced functional deficits following spinal cord ischemia in a rabbit model.

Recombinant NGF has been tested in phase II and phase III clinical trials for the treatment of patients with small fiber neuropathies. In a phase II trial with AIDS patients, it was reported that NGF-treatment caused significant relief of deafferentiation pain. McArthur et al. ((2000) *Neurology* 54:1080).

Copies of Tuszynski, De Rosa, Bowes, and McArthur are provided herewith.

In view of the data presented in the instant application, and in view of the disclosure in the literature, those skilled in the art would find it reasonable that administration of a trk agonist, such as a multivalent Ig that activates trk, would be efficacious in treating disorders amenable to treatment with NGF.

Conclusion as to the rejection under 35 U.S.C. §112, first paragraph

Applicants submit that the rejection of claims 7-15 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCSF-305CON4.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: Jan. 18, 2008

By: _____
Paula A. Borden
Registration No. 42,344

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Facsimile: (650) 327-3231

F:\DOCUMENT\UCSF\305con4\Response_091207OA.doc